Updates on COVID-19 Vaccines

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Disclosures

- No financial disclosures.
- I do not intend to discuss unapproved/investigative use of commercial products (pending FDA approval process for pediatrics).

Objectives

- Learn current status and updates of COVID-19 and its complications in pediatric patients
- Identify important updates in COVID-19 vaccines
- Describe current vaccine strategies, including use of boosters, for SARS-CoV-2

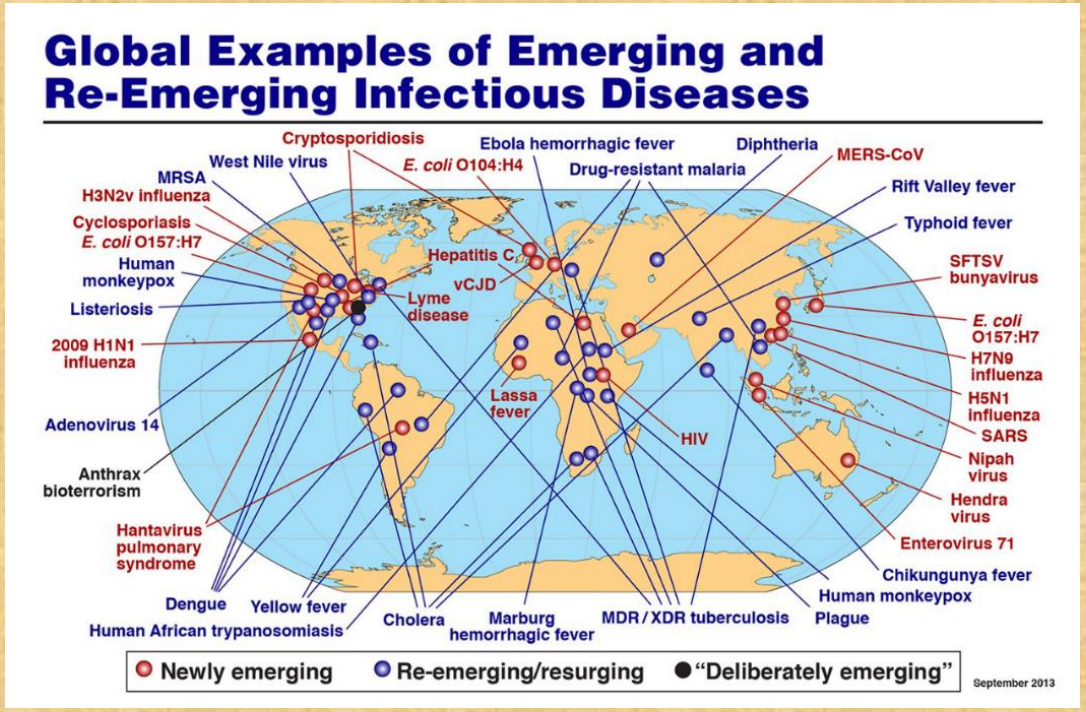
“The most likely forecast about the future of infectious diseases is that it will be very dull…”

“There is always a risk of some wholly unexpected emergence of a new and dangerous infectious disease, but nothing of the sort has marked the last fifty years.”

- Macfarlane Burnet and David White, 1972

Infection outbreaks after 1972

- Herpes Simplex Virus
- Legionnaires' Disease
- AIDS
- SARS (SARS-CoV-1)
- Ebola
- MERS
- Influenza H1N1
- COVID-19

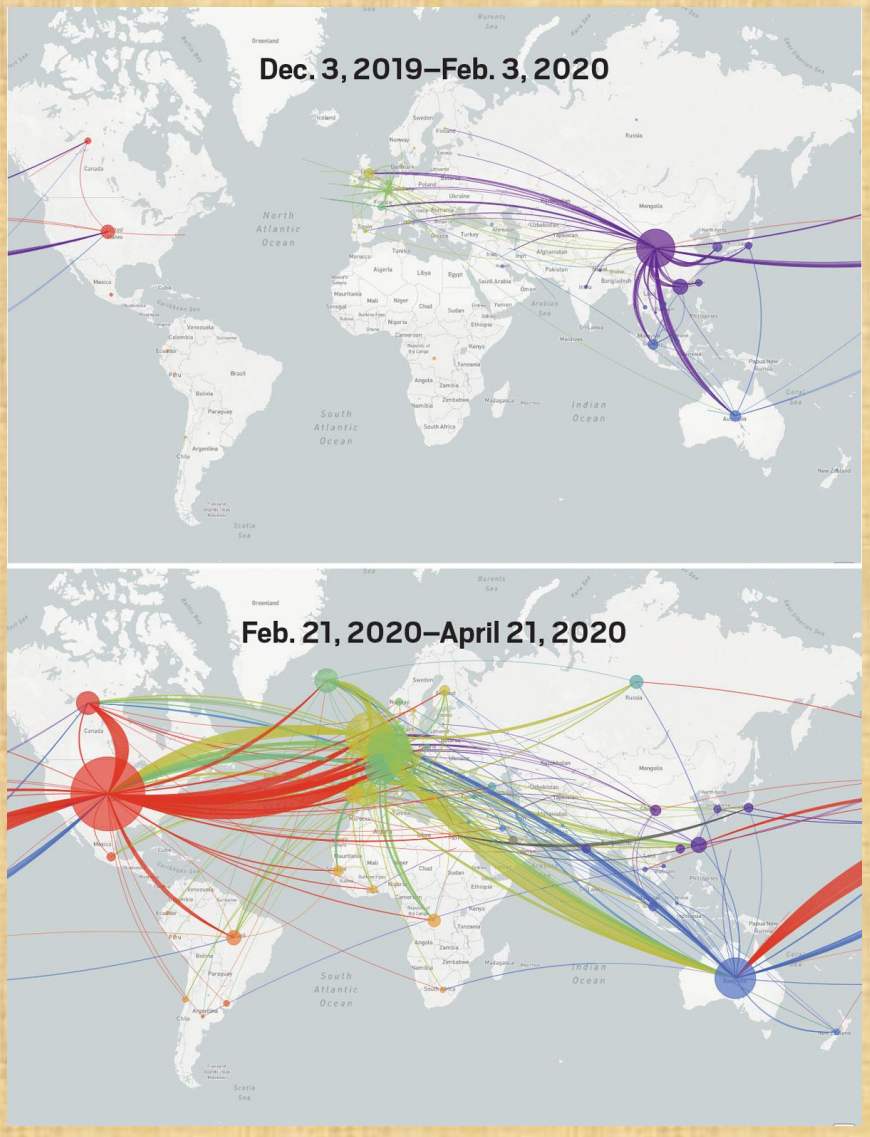


COVID-19: The Early Days

- Wuhan Province, China – December 2019
- March 11, 2020: pandemic declared
- Wuhan experience:
  - 72,000 patients:
    - 81% mild
    - 14% severe
    - 5% critical
  - Risk factors: older age, comorbidities
  - Mortality: 2.3%
  - (Influenza mortality: 0.1%)

World Health Organization

COVID-19 Global Spread

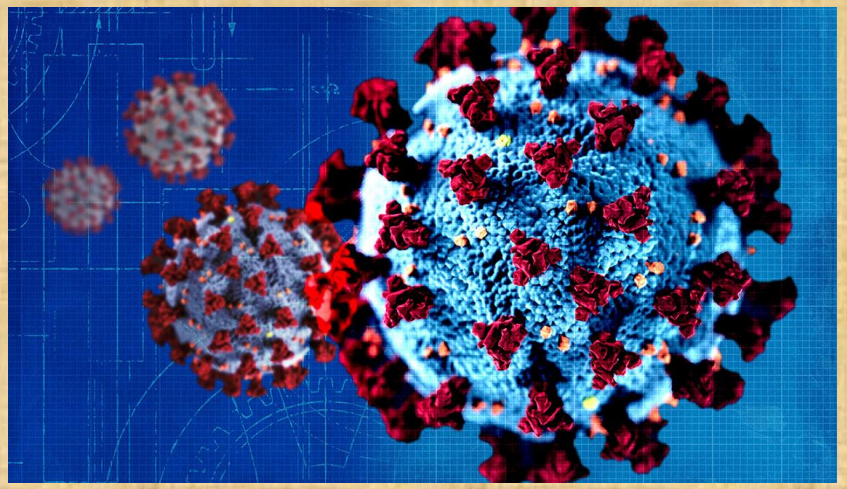


COVID-19: Today (3/10/2023)

- World:
  - 676,609,955 cases
  - 6,881,955 deaths
  - 13,338,833,198 total vaccine doses administered
- U.S.:
  - 103,804,263 cases
  - 1,123,836 deaths
- Maricopa county: 1,530,296 cases (#4 in U.S.)
- Pediatric cases:
  - 15,493,835 cases
  - 20,585 cases/100,000 children

COVID-19: The Variants

- Variants of Concern:
  - B.1.1.7 (UK, “Alpha”)
  - B.1.351 (S. Africa, “Beta”)
  - B.1.617.2 (India, “Delta”)
  - **B.1.1.529 (S. Africa, “Omicron”)**
- Sub-variants of Omicron:
  - B.A. 2, 4, & 5
  - BQ.1 and BQ.1.1 (15%)
  - XBB.1.5 (“Kraken”, 82%)
  - CH.1.1 (“Orthrus”, 1.7%)



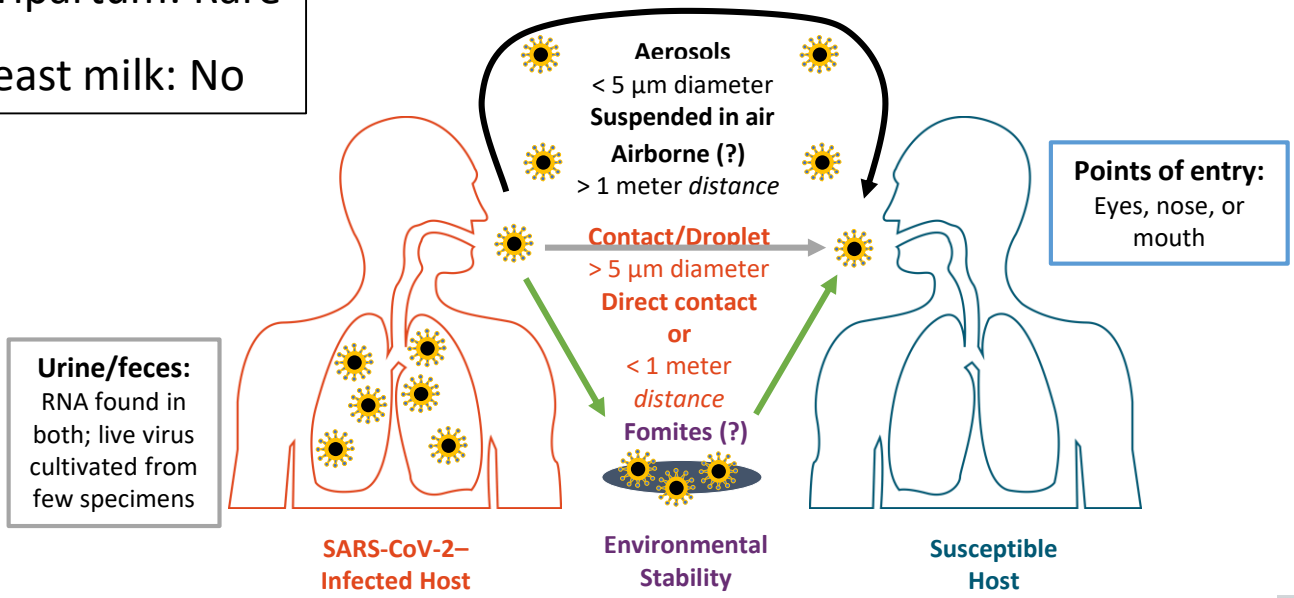
Omicron Variant – B.1.1.529 (B)

- S. Africa and Botswana
- Origin in a single patient?
- Mutations:
  - 50 novel single-mutations
  - 30 – Spike protein
  - 10 – Active binding site
- More transmissible: 70-fold faster replication
- Less virulent????
- Combination event with Coronavirus OC43?

Proposed Routes of SARS-CoV-2 Transmission

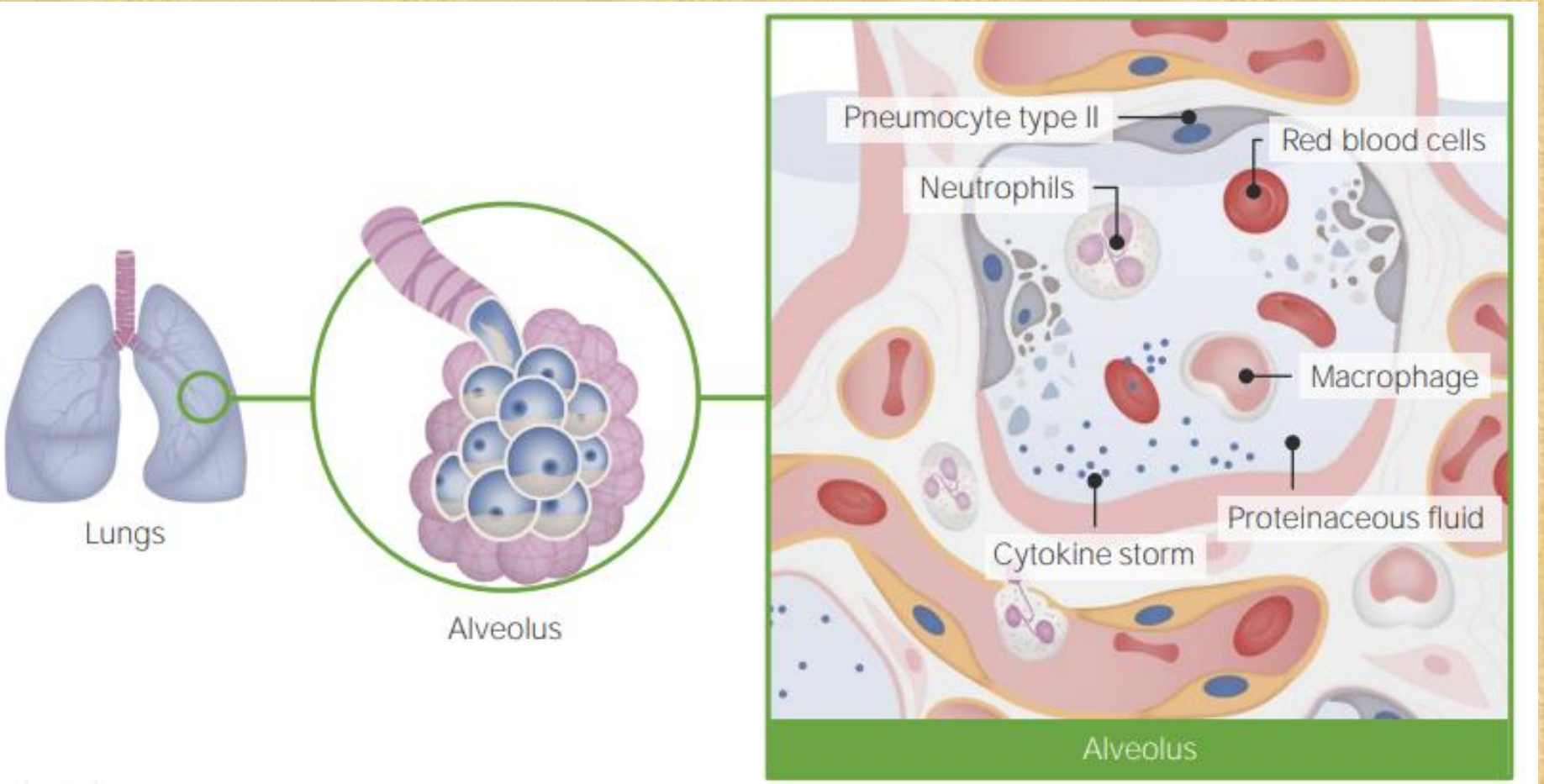
Peripartum: Rare

Breast milk: No



Galbadage. Front Public Health. 2020;8:163. WHO. Scientific Brief. July 9, 2020.

Slide credit: clinicaloptions.com


Lungs
Alveolus
Pneumocyte type II
Red blood cells
Neutrophils
Macrophage
Proteinaceous fluid
Cytokine storm
Alveolus

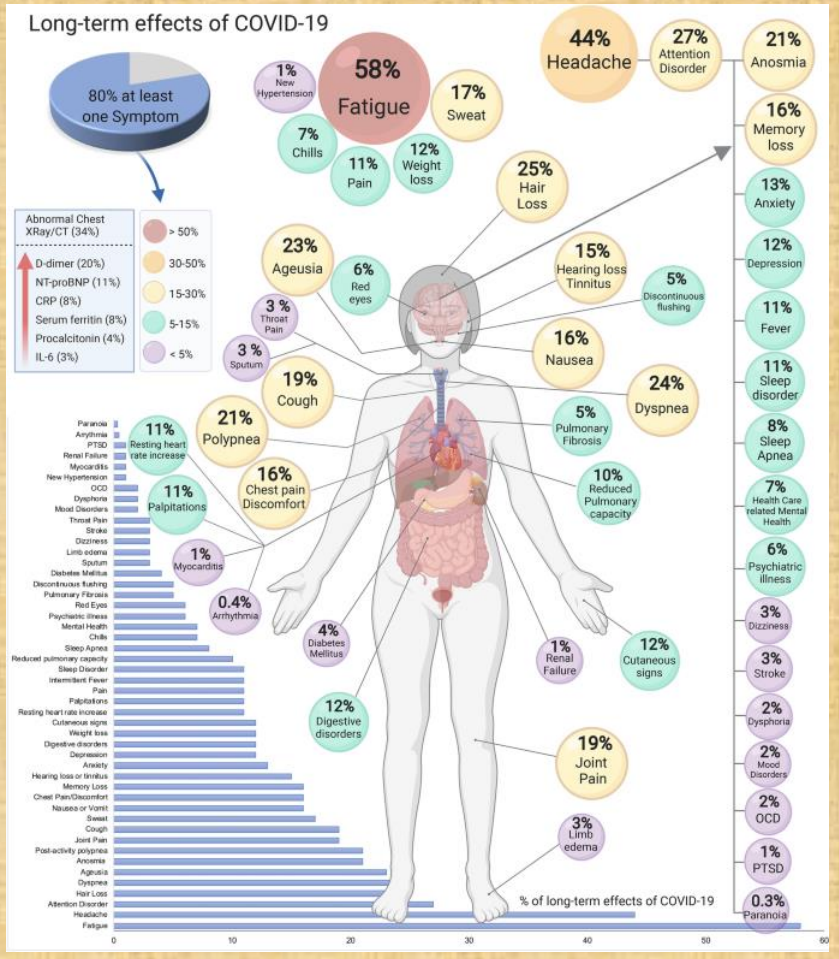
COVID-19 Clinical - Omicron

- **Mild disease:**
  - Fevers
  - Muscle aches
  - Malaise
  - Congestion, RN
  - Sore throat
  - ~~Shortness of breath~~
  - ~~Anosmia~~
  - Incubation period: ??
  - Length: 3 – 7 days

- **Severe disease:**
  - ~~Dyspnea~~
  - ~~Respiratory failure~~
  - ~~High cardiac-output shock~~
  - ~~Multi-organ inflammation~~
  - ~~Coagulopathy~~
  - ~~“Hyperimmune” disease~~
  - Croup
  - Combination disease

COVID-19 Complications

- Post-Acute COVID-19 Syndrome:
  - Fatigue
  - Myocarditis
  - Headaches
  - Cognitive dysfunction
  - Chronic lung disease
  - anosmia
- MIS-C
- Mental Health Crisis



MIS-C Case Definition (CDC)

- Fever (≥ 38.0 C for ≥ 24 hours)
- Laboratory evidence of inflammation (CRP, ESR, Fibrinogen, PCT, d-dimer, ferritin, LDH)
- Severe illness requiring hospitalization
- Multisystem organ involvement (≥ 2: cardiac, renal, respiratory, hematologic, GI, derm, neuro)
- No alternate, plausible diagnosis
- + current/recent SARS-CoV-2 infection OR COVID-19 exposure within prior 4 weeks

MIS-C: Case series 2020-2021

- Clinical findings:
  - **GI symptoms (97%)**
  - Shock (76%)
  - Acute kidney injury (70%)
  - **Neurocognitive symptoms (58%)**
  - **Myocardial involvement (58%)**
  - O2 requirement (52%)
  - Respiratory symptoms (52%)
  - Coronary artery abnormalities (48%)
  - **Elevated inflammatory markers: CRP, Fibrinogen, PCT, Ferritin, LDH**
  - **Lymphopenia/Neutrophilia**
- Kawasaki-like???

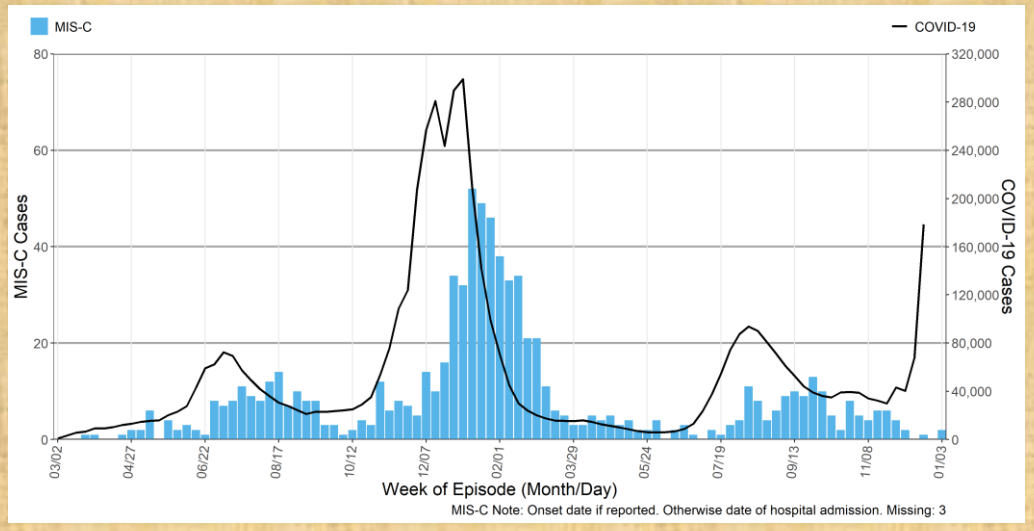
MIS-C Treatment

- Evaluation
- Aspirin – low dose
- IVIG
- Steroids
- mAb??
- Plasmapheresis??

- ESR, CRP, PCT
- D-dimer, INR, PT/PTT, Fibrinogen
- Ferritin
- Troponin, NT-proBNP
- SARS-CoV-2 NAAT, COVID-19 Ab
- ECG
- ECHO?

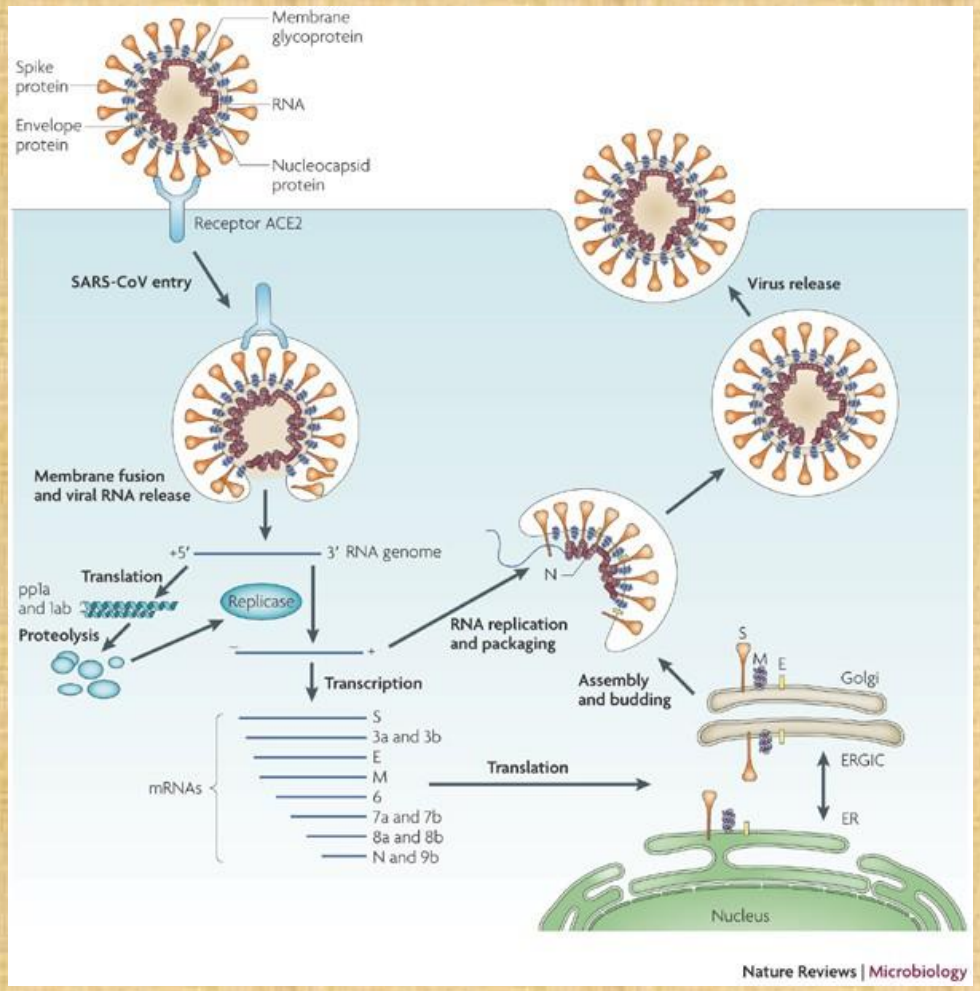
MIS-C Next…??

- Outcomes:
  - 100% cardiac injury
  - 98% GI presentation
  - Resolved by 3 months
  - Clinical recovery 1 – 2 months
- New MIS-C cases??



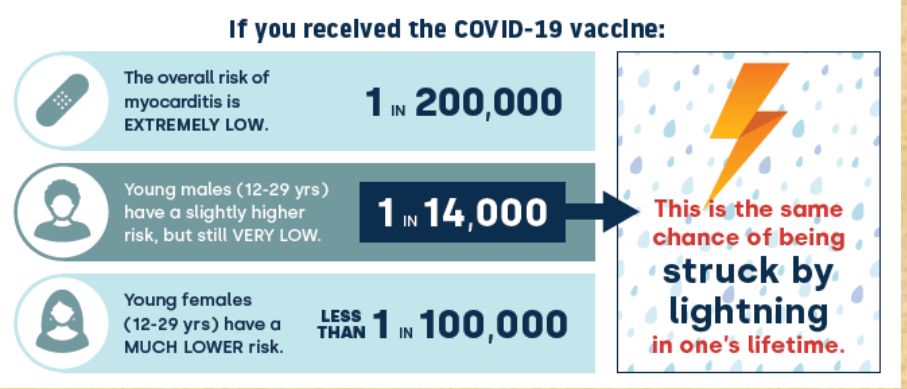
COVID-19: Treatment

- Antiviral agents:
  - Remdesivir
  - Molnupiravir
  - Paxlovid:
    - PF-07321332
    - Ritonavir
- Other stuff:
  - Azithromycin
  - Vit. D, C; Zinc
  - Hydroxychloroquine
  - Ivermectin



COVID-19: Treatment

- Immunomodulatory therapy:
  - Dexamethasone
  - Other steroids?
  - ~~Convalescent plasma~~
  - ~~Monoclonal antibodies~~
  - Baricitinib: selective Janus kinase 1/2 inhibitor
- Vaccines:
  - mRNA – monovalent vs bivalent (Pfizer/Moderna)
  - Nanoparticle-Spike protein (Novovax)
- Safety

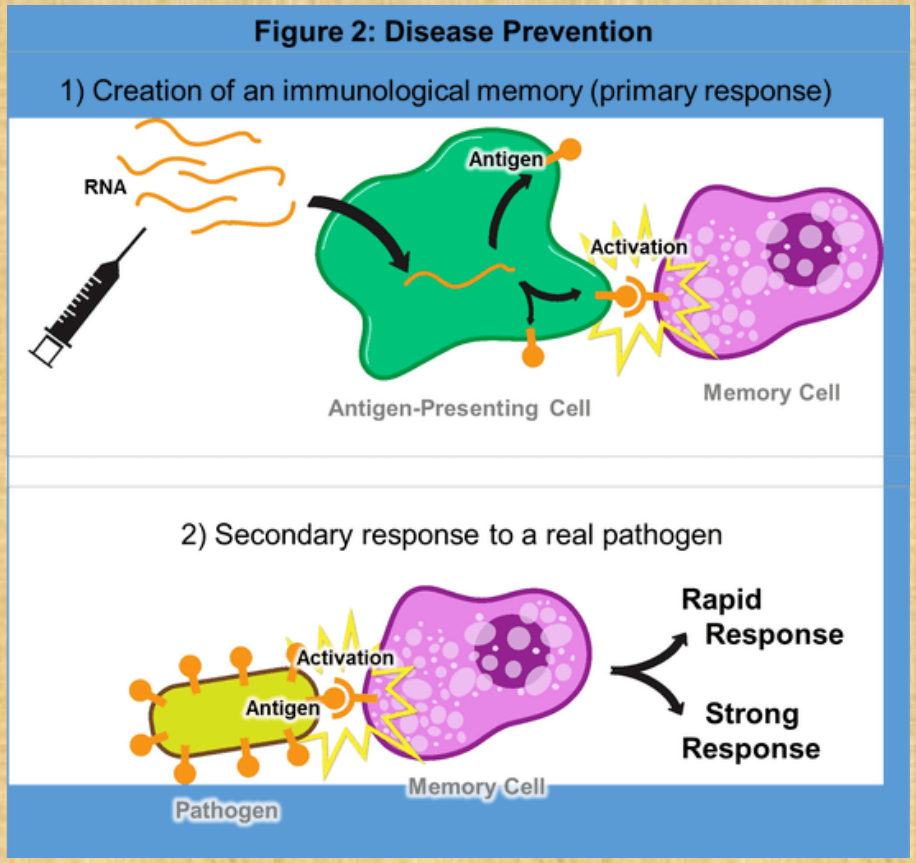


COVID-19: Prevention

- Vaccines – Operation Warp Speed:
  - mRNA (Moderna, Pfizer)
  - Replication-deficient Adenovirus (AstraZeneca, Janssen)
  - Spike-protein/nanoparticles (Novavax)
  - Sputnik-V (Ad5-vector)
  - CoronaVac (Sinovac-China; inactivated)
  - Live-attenuated virus & polysaccharide-based vaccines
  - Intranasal vaccines (UK, China)

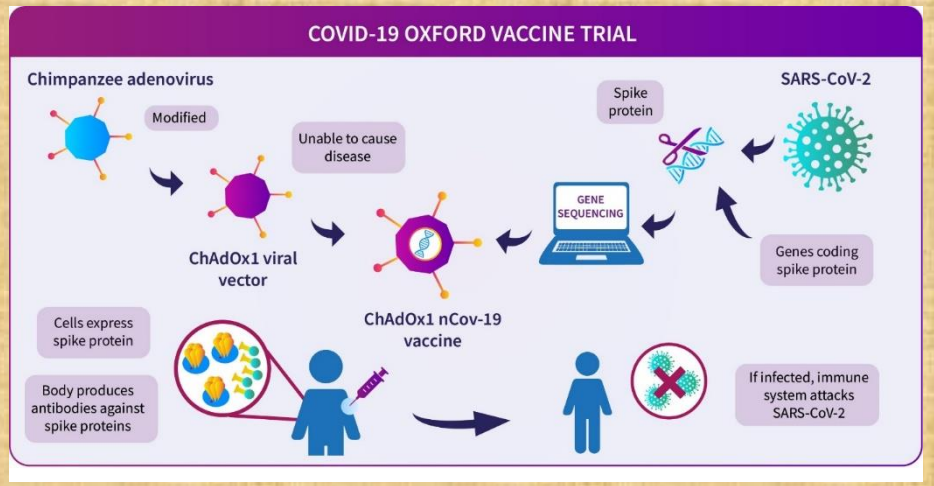
RNA vaccines

- Pfizer & Moderna
- Inert
- Two injections
- Efficacy 94% (initial)
- Side-effects



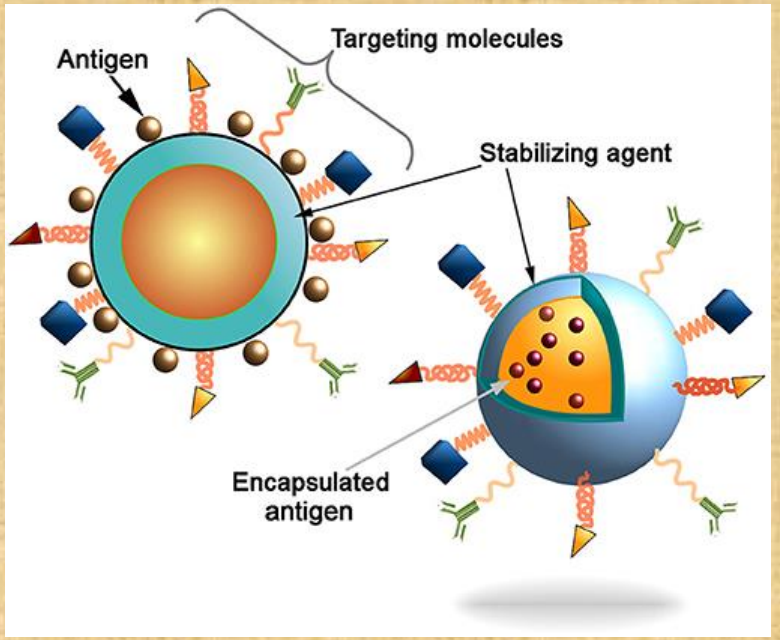
Vectored Vaccines

- Adenovirus = vector
- AstraZeneca, Janssen (Johnson & Johnson), Sputnik V, etc.
- Recent History with Ad vectors
- 1 vs 2 injections
- Efficacy 71% (initial)
- Side-effects



Nanoparticle vaccine

- Spike protein stabilized by nanoparticles
- Novavax
- Status
- Efficacy 91% (initial)
- Side-effects



COVID-19: Prevention

- Vaccines – Operation Warp Speed:
  - **mRNA (Moderna, Pfizer)**
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COVID-19: Pediatric Vaccines

- Pfizer mRNA - Monovalent
  - Full approval: 16 years +
  - EUA – Adolescent dose (30 mcg): 12 years – 15 years
  - EUA – Pediatric dose (10 mcg): 5 years – 11 years
  - EUA – Infant dose (3 mcg): 6 months – 4 years
- Moderna mRNA - Monovalent
  - Full approval: 18 years +
  - EUA – Infant and Pediatric : 6 months – 17 years

COVID-19: Pediatric Boosters

- Pfizer:
  - Bivalent booster: 5 years – 17 years
  - > 2 mo. after primary series
  - NEW bivalent booster recommendation (EUA): 6 months – 4 years
  - Primary series (3 doses: 6 mo – 4 yrs)
- Moderna:
  - Bivalent booster: 6 months – 17 years
  - 2 months after primary series (2 doses)
- Pfizer or Moderna bivalent booster: ≥ 6 y.o.

COVID-19: Pediatric Boosters

- Novavax:
  - No booster
  - Primary series = 2 doses ages ≥ 12 y.o.
  - Moderna or Pfizer bivalent booster
  - Booster > 2 months after primary Novavax series

Birth to 15 Months

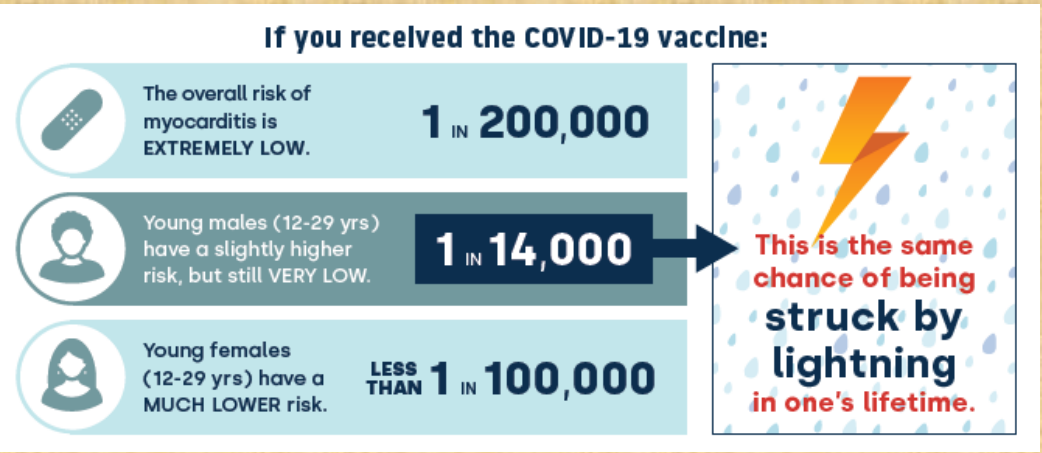
Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos
Hepatitis B (HepB)	1st dose	←2nd dose→			←3rd dose→			
Rotavirus (RV) RV1 (2-dose series); RV5 (3-dose series)			1st dose	2nd dose	See notes			
Diphtheria, tetanus, & acellular pertussis (DTaP: <7 yrs)			1st dose	2nd dose	3rd dose			←4th dose→
Haemophilus influenzae type b (Hib)			1st dose	2nd dose	See notes		←3rd or 4th dose, See notes→	
Pneumococcal conjugate (PCV13, PCV15)			1st dose	2nd dose	3rd dose		←4th dose→	
Inactivated poliovirus (IPV: <18 yrs)			1st dose	2nd dose	←3rd dose→			
COVID-19 (1vCOV-mRNA, 2vCOV-mRNA, 1vCOV-aPS)					2- or 3-dose primary series and booster (See notes)			
Influenza (IIV4)					Annual vaccination 1 or 2 doses			
or Influenza (LAIV4)								
Measles, mumps, rubella (MMR)					See notes		←1st dose→	

18 Months to 18 Years

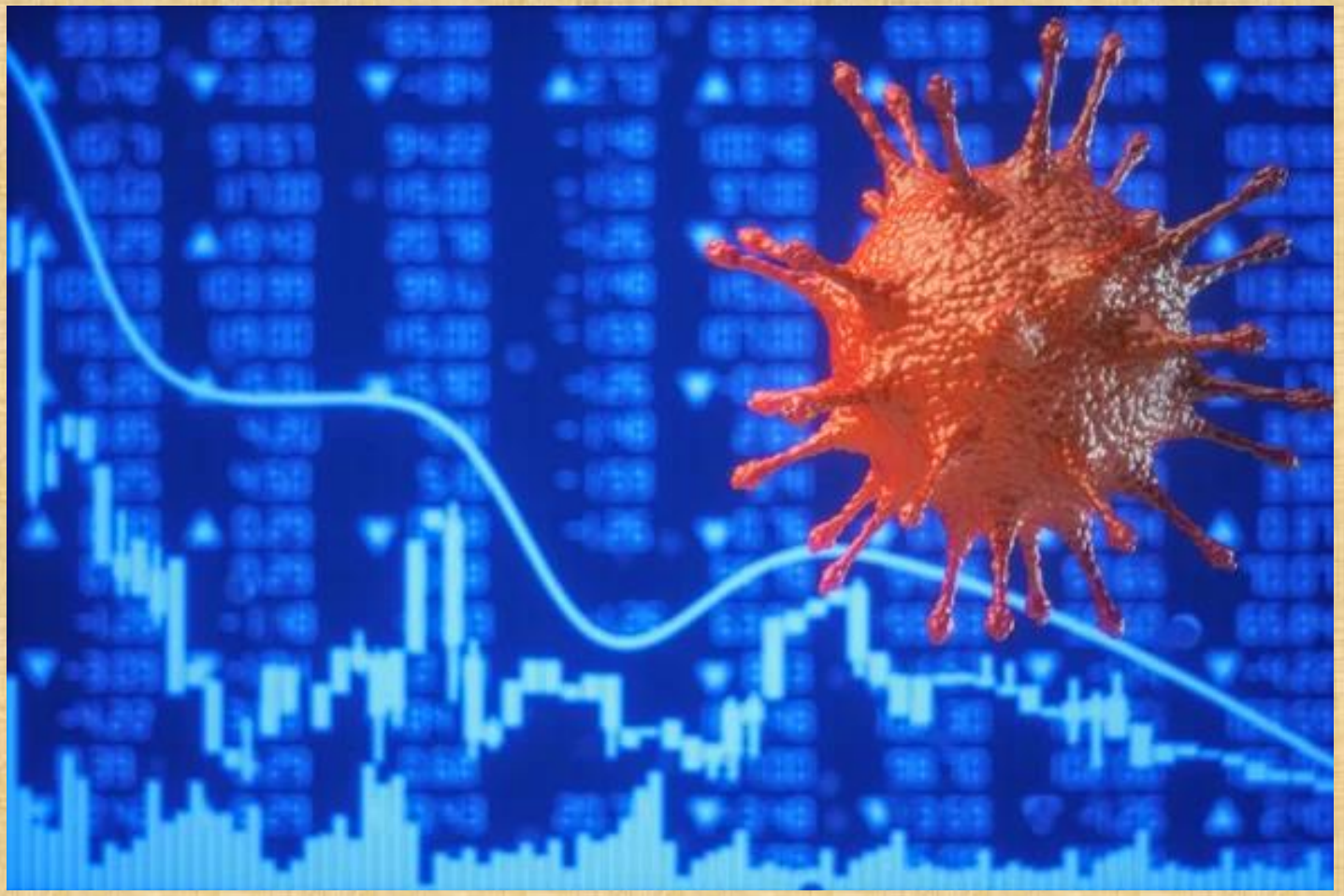
Vaccines	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16 yrs	17-18 yrs
Hepatitis B (HepB)	←3rd dose→								
Rotavirus (RV) RV1 (2-dose series); RV5 (3-dose series)									
Diphtheria, tetanus, & acellular pertussis (DTaP: <7 yrs)	←4th dose→			5th dose					
Haemophilus influenzae type b (Hib)									
Pneumococcal conjugate (PCV13, PCV15)									
Inactivated poliovirus (IPV: <18 yrs)	←3rd dose→			4th dose					See notes
COVID-19 (1vCOV-mRNA, 2vCOV-mRNA, 1vCOV-aPS)	2- or 3- dose primary series and booster (See notes)								
Influenza (IIV4)	Annual vaccination 1 or 2 doses					Annual vaccination 1 dose only			
or Influenza (LAIV4)			Annual vaccination 1 or 2 doses			or Annual vaccination 1 dose only			
Measles, mumps, rubella (MMR)				2nd dose					

COVID-19: Prevention

- Vaccine safety concerns:
  - Anaphylaxis & Allergic reactions
  - Neurologic effects (GBS, BP)
  - Pregnancy and Nursing
  - Thrombotic events
  - Myocarditis:
    - Healthy young men
    - A-fib



COVID-19: The Future



"We've been hitting the snooze button on emerging diseases for decades. The alarm is going off and it's time to wake up."

-Dr. Anne Rimoin, Epidemiologist- UCLA


56M
Smallpox
1520
40-50M
Spanish Flu
1918-1919
30-50M
Plague of Justinian
541-542
25-35M
HIV/AIDS
1981-PRESENT
12M
The Third Plague
1855
6.3M*
COVID-19
2019-10:00AM PT,
JULY 08, 2022
[ONGOING]
5M
Antonine
Plague
165-180
3M
17th Century
Great Plagues
1600
1.1M
Asian Flu
1957-1958
1M
Russian Flu
1889-1890
1M
Hong Kong Fl
1968-1970
1M
Cholera 6
outbreak
1817-1923
1M
Japanese
Smallpox Epidemic
735-737
600K
18th Century
Great Plagues
1700
200K
Swine Flu
2009-2010
100-150K
Yellow Fever
LATE 1800s
11.3K
Ebola
2014-2016
850
MERS
2012-PRESENT
770
SARS
2002-200